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Has the ADHD phenotype become more common in children between 2004 and 2014? Trends over 10 years from a Swedish general population sample

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Abstract

Background: Studies have reported increases in clinically diagnosed and treated Attention deficit hyperactivity disorder (ADHD) during the last decade, but it is unclear if this reflects an increase in the underlying ADHD phenotype. We aimed to clarify if there has been an increase in the prevalence of ADHD-like traits in the general population from 2004 to 2014.

Method: Data were collected from 19,271 nine-year old twins, participating in the population-based Child and Adolescent Twin Study in Sweden between 2004 and 2014. We assessed lifetime ADHD symptoms using the Autism-Tics, ADHD and other Comorbidities inventory. Research proxies for *diagnostic level ADHD* and *subthreshold ADHD* were derived from this scale. We modelled the lifetime prevalence of diagnostic level and subthreshold ADHD with logistic regression, and assessed mean ADHD scores each year with linear regression. Lifetime prevalence of clinically diagnosed ADHD was retrieved from the National Patient Register and modelled with logistic regression.

Results: The prevalence of diagnostic level ADHD based on parent ratings did not differ significantly over time from 2004 to 2014 (OR 1.37; 95% CI: 0.77-2.45; p-value .233). Both subthreshold ADHD and mean ADHD scores increased significantly over time (both p-values < .001). Clinically diagnosed ADHD increased more than five-fold from 2004 to 2014 (OR 5.27, 95% CI 1.85-14.96).

Conclusion: We found no evidence of an increase of ADHD-like traits at the extreme end of the distribution from 2004-2014, but small increases in normal and subthreshold variations of ADHD-like traits were observed. This suggests that the increased rates of clinically diagnosed ADHD might reflect changes in diagnostic and treatment practices of ADHD, administrative changes in reporting diagnoses, greater awareness of ADHD, better access to healthcare, or current over-diagnosis, rather than an increase in the ADHD phenotype.

Keywords: ADHD; epidemiology; time trends; lifetime prevalence

INTRODUCTION

Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder, with a worldwide prevalence of around 5% (Polanczyk, de Lima, Horta, Biederman & Rohde, 2007). ADHD is usually diagnosed in childhood, with a higher prevalence among boys than girls, and is more common in lower socio-economic strata (Biederman & Faraone, 2005). Furthermore, at least half of the children with ADHD continue to have impairing symptoms as adults (Biederman et al., 2005), and it is associated with adverse outcomes such as poor school achievement, financial problems, criminality, accidents, substance use disorder and an increased risk of psychiatric problems (Klein et al., 2012).

Several studies from different countries suggest that the prevalence of clinically diagnosed ADHD has increased substantially over time. In a population-based study from Finland, Denmark and Sweden, Atladottir et al. found that the age-specific prevalence of clinically diagnosed ADHD increased among 10-year olds in all three countries (1.83-fold in Finland, 2.95-fold in Denmark and 7.21-fold in Sweden) during the period 1990 to 2007 (Atladottir et al., 2015). In a Swedish population-based study, Giacobini et al. showed that the one-year prevalence of clinical diagnoses increased more than four-fold, and the annual incidence increased more than two-fold, from 2006 to 2011 (Giacobini, Medin, Ahnemark, Russo & Carlqvist, DOI: 10.1177/1087054714554617). A similar trend has been shown in a Taiwanese study based on insurance records, with a 27-fold increase in the one-year prevalence of clinically diagnosed ADHD in children from 1996 to 2005, and a 17-fold increase in the incidence from 1997 to 2005 (Chien, Lin, Chou & Chou, 2012). Similar patterns have been found in the US as well. In studies based on surveys conducted with US office-based physicians, the one-year prevalence of clinical diagnoses among 5-18 years old children increased three-fold from 1990 to 1998 (Robison, Skaer, Sclar & Galin, 2002), and the

biannual prevalence increased four-fold from 1991 to 2008, when the same data was analyzed ten years later (Sclar et al., 2012). Similarly, the lifetime prevalence of diagnosed ADHD increased with 42% from 2003 to 2011 in a population-based study of 4-17 year old children, where parents were asked to report whether their children had ever received an ADHD diagnosis by a physician (Visser et al., 2014).

A similar trend has been documented for the prevalence of dispensed ADHD medication, both in Sweden (Zetterqvist, Asherson, Halldner, Långström & Larsson, 2013) and in other western countries (Renoux, Shin, Dell'Aniello, Fergusson & Suissa, 2016, Beau-Lejdstrom, Douglas, Evans & Smeeth, 2016, Zito et al., 2003, Trip, Visser, Kalverdijk & de Jong-van den Berg, 2009). The one-year prevalence of dispensed ADHD medication has increased 7.5-fold from 1996 to 2006 in the Netherlands (Trip et al., 2009), and 2.28-fold from 2006-2009 in Sweden (Zetterqvist et al., 2013), based on population-based registers of prescribed medication. Data from insurance records in the US similarly showed a two to three-fold increase in the one-year prevalence of dispensed ADHD medication among children during the period 1987 to 1996 (Zito et al., 2003). Similarly, two studies of patients registered in a medical records database in the UK, have shown that the one-year prevalence of prescribed ADHD medication increased 34-fold among children from 1995 to 2013 (Beau-Lejdstrom et al., 2016), and almost nine-fold among all 6-45 year old patients 2000 to 2015 (Renoux et al., 2016).

Despite the different study populations and different methods used, these previous studies all point towards increasing rates of clinically diagnosed and treated ADHD. However, it has been suggested that even though rates of clinically diagnosed ADHD have increased, ADHD symptoms seem to have been stable over time (Safer, DOI: 10.1177/1087054715586571),

which suggests that the increase seen in studies based on clinical diagnosis does not necessarily reflect an increase in the underlying ADHD phenotype. Changes in quality of data, and administrative changes in reporting diagnoses, are plausible alternative explanations. Greater awareness about ADHD among physicians, as well as among parents and teachers, is also a likely explanation for the increase in diagnosed and treated ADHD. A greater awareness among physicians could also have resulted in fewer misdiagnosed individuals, and more individuals receiving proper treatment. Furthermore, better access to healthcare might explain the increase seen in some countries (Chien et al., 2012). This increase might also be influenced by changes in the classification systems used as the diagnostic criteria for ADHD has evolved over a period of 20-30 years, (Faraone, Sergeant, Gillberg & Biederman, 2003) which gradually causes changes in diagnostic practice.

To explore potential changes in the prevalence of ADHD over time, Polanczyk et al. recently conducted a large meta-analysis of non-referred samples, based on 135 worldwide studies conducted during a period of 30 years (Polanczyk, Willcutt, Salum, Kieling & Rohde, 2014). This study found no evidence of an increase in the prevalence of ADHD, speaking against an increase in the underlying ADHD phenotype. However, the meta-analysis had some limitations as several different measures of ADHD were used in the studies (including e.g. both clinical diagnosis as well as parental reports), individuals in different ages were included, and publication year was used as a proxy since information about which year the study was conducted was not always available (Polanczyk et al., 2014).

There is a need for studies based on cohorts of individuals of the same age, conducted in the same location for a longer period of time, using a stable and validated measure of ADHD. In this study, we aimed to clarify if the lifetime prevalence of ADHD-like traits in nine year old

children has increased in Sweden during the last decade. Based on the meta-analysis by Polanczyk et al., where no increase was found in the prevalence of ADHD in population-based samples worldwide, we hypothesized that the underlying ADHD phenotype has been stable over time.

METHODS

Study population and data collection

Data were collected from participants in the Child and Adolescent Twin Study in Sweden (CATSS). CATSS is an ongoing study of all nine-year old twins in Sweden, and was initiated in 2004 with the purpose to study physical and mental health problems in twins during childhood and adolescence (Anckarsäter et al., 2011). Parents of all twins in Sweden are contacted during the year the twins turn 9 and asked to participate in a telephone interview (see below). Parents of 27,820 children (13,910 twin pairs) born from 1st of July 1995 to 31st of December 2005 were asked to participate in CATSS during the years 2004-2014. Of these, parents of 19,358 twins (corresponding to 9,679 pairs) participated, yielding an overall response rate of 69.6%. Non-responders were more likely than responders to have a parent treated in psychiatric clinics, a parent convicted of a crime, divorced parents, or to belong in low socio-economic strata (Anckarsäter et al., 2011). Non-responders also had higher prevalence of disorders such as ADHD (2.1% versus 1.6%), and higher prevalence of prescribed ADHD medication (1.8% compared with 1.4%) (Anckarsäter et al., 2011). Individuals with missing information on ADHD were excluded from the analysis (n=87), yielding a final analytical sample of 19,271 children from 9,673 families. Parents gave their informed consent for themselves and their children to participate in the study. The study was approved by the Regional Ethical Review Board in Stockholm (DNR: 02-289 and 2010/597-31/1).

Measures

Data on ADHD traits were assessed using the Autism-Tics, ADHD and other Comorbidities inventory (A-TAC) (Hansson et al., 2005), which was administered to parents. A-TAC is an instrument that was developed to measure child and adolescent mental health problems in large-scale epidemiological studies, based on telephone ratings conducted by lay interviewers. The instrument was developed to capture DSM-IV symptom descriptions. The ADHD-scale consists of 19 statements, each with the following response options: "no", "yes, to some extent", and "yes" (coded as 0/0.5/1). These statements are asked in a lifetime perspective, i.e. parents are asked to consider if the child either has these problems/difficulties currently, or earlier in life. These 19 items were summarized into a total index for all individuals who responded to at least 17 items, thereby ranging from 0 to 19. The scale has been shown to have good reliability, with intraclass coefficients of 0.89 and 0.84 for intra-rater and inter-rater respectively, and a Cronbach's α of 0.92 (Larson et al., 2014, Anckarsäter et al., 2011). The ADHD scale also consists of two subscales, measuring the two dimensions of ADHD: attention deficit/concentration, which consists of 9 items and ranges from 0-9, and hyperactivity/impulsivity, consisting of 10 items and thereby ranging from 0 to 10. A cut-off of ≥12.5 on the ADHD-scale has been clinically validated to correspond to a clinical research diagnosis of ADHD (*diagnostic level ADHD*). This cut-off had a sensitivity of 0.56 and specificity of 0.93 when clinical cases were compared cross-sectionally to controls, and a sensitivity of 0.20 and specificity of 0.97 when assessed in a clinical longitudinal follow-up study(Larson et al., 2010, Larson et al., 2013). Moreover, a cut-off of ≥6 has been used to identify subthreshold ADHD, used for screening diagnosis in surveys. This cut-off had a sensitivity of 0.91 and specificity of 0.73 in cross-sectional comparisons of clinical cases and controls, and a sensitivity of 0.64 and specificity of 0.78 when assessed in a clinical

longitudinal follow-up study (Larson et al., 2010, Larson et al., 2013). These two categorical measures were not mutually exclusive; individuals with a score ≥12.5 were considered to fulfill the criteria for diagnostic level ADHD, as well as for subthreshold ADHD.

The items measuring ADHD in A-TAC have been the same over time and were asked by laymen without any clinical knowledge. Furthermore, the scale was constructed to not disclose which questions measured which disorder, and parents were asked to rate their children on specific symptoms, rather than report if their child had a diagnosis. Taken together, this reduced the risk of bias caused by diagnostic substitution, changes in diagnostic criteria or clinical practice, or from increased awareness of ADHD.

In this study, we used three different measures to study trends in the lifetime prevalence of the ADHD phenotype over time. First, our main analyses were based on the categorical measure previously validated to capture diagnostic level ADHD. We considered an increase in diagnostic level ADHD to be clinically relevant. Second, in order to further assess a potential increase in the underlying ADHD phenotype, we also assessed the lifetime prevalence of subthreshold ADHD over time. Third, in order to investigate changes at the general symptom level over time, we assessed the mean scores on the ADHD-scale, including the two subscales, over time.

Clinically diagnosed ADHD based on registers

Since previous attrition analysis has shown that non-responders were more likely to receive an ADHD diagnosis than responders (Anckarsäter et al., 2011), and since participation in CATSS has declined over time, we were concerned that attrition might influence the trends of prevalence studied. Therefore, we performed a sensitivity analysis based on linkage of

national Swedish registers. Due to the linkage with national registers, these numbers differ slightly from the number of individuals eligible and participating in CATSS. In total, we identified 28,378 twins born in Sweden between 1st of July 1995 and 31st of December 2005. Twins who had died or emigrated before turning nine years old were excluded (n=1,220), resulting in a sample size of 27,158 nine-year old twins who were living in Sweden when they were nine years old (2004-2014). Of these, 19,041 participated in CATSS. Through record linkage with the National Patient Register (Ludvigsson et al., 2011) we identified children who had received at least one ADHD diagnosis (ICD-9: 314; ICD-10: F90) by a physician before age 10.

Data analysis

SAS version 9.4 for Windows (SAS Institute Inc., Cary, N.C., USA) and Stata Statistical Software: Release 13 (StataCorp. 2013. College Station, TX: StataCorp LP) were used for all analyses.

We used logistic regression to model the lifetime prevalence rate of diagnostic level ADHD each year with corresponding 95% Confidence Intervals (CI). To further describe the potential increase in the ADHD phenotype throughout the study period, we used logistic regression to calculate an odds ratio (OR), comparing the prevalence the first year of study with the last year. In secondary analysis, we modelled the lifetime prevalence of subthreshold ADHD in a similar manner. Furthermore, we used linear regression models to assess the effect of year on mean ADHD scores (and corresponding 95% CIs). Mean scores on the subscales attention deficit/concentration and hyperactivity/impulsivity were similarly analyzed. To assess potential differences between boys and girls, we repeated all analyses stratifying for sex.

Cluster robust sandwich standard errors (Stefanski & Boos, 2002) were used in all analyses to account for non-normality in data and dependence between observations.

Sensitivity analyses

Since twins provide correlated responses, and symptoms might be more likely to be noted in one twin if the other is already diagnosed, we repeated the analyses in a subsample consisting of one randomly selected twin per pair (n=9,673).

To investigate the potential influence of attrition on trends in prevalence, we used logistic regression to model the lifetime prevalence of clinically diagnosed ADHD each year, including an interaction term of year and participation in CATSS. We also used this record linkage to model the lifetime prevalence of clinically diagnosed ADHD among participants in CATSS, in order to compare changes over time in the underlying phenotype (diagnostic level ADHD) with ADHD diagnosed by clinicians. It was not possible to analyze clinically diagnosed ADHD separately for boys and girls since too few girls had a diagnosis (n=69).

[Insert Table 1 about here]

RESULTS

Table 1 presents descriptive statistics for twins participating in CATSS 2004 to 2014, separately for those born 1995-1998, 1999-2002 and 2003-2005. Of the 19,271 participants, 50.6% were boys (n=9,759) and 49.4% were girls (n=9,512). Over the ten year study period, 2.1% (n=406) of participants fulfilled the criteria for diagnostic level ADHD (i.e., had a score of 12.5 or more on the ADHD scale). The corresponding proportion of individuals with subthreshold ADHD (ADHD score of 6 or more) was 10.7% (n=2,058). The mean score on

the ADHD scale was 2.04 (standard deviation, sd: 3.11), with mean values of 1.03 (sd: 1.74) and 1.00 (sd: 1.69) on the two subscales attention deficit/concentration and hyperactivity/impulsivity respectively. The distribution of ADHD scores over time (categorized as 0; 0.5-3; 3.5-5.5; 6-12; and ≥12.5) is shown in Figure S1 (available online). Overall, there was no clear difference over time at the extreme end of the distribution, whereas there seemed to be a shift towards slightly increased scores at the normal and subthreshold level.

[Insert Table 2 about here]

The lifetime prevalence of diagnostic level and subthreshold ADHD is presented in Figure 1 and Table 2. There was no significant difference in the prevalence of diagnostic level ADHD over time (p-value: .233). The prevalence fluctuated around 2% most years, with the lowest value in 2009 (1.42%; 95% CI: 0.82-2.01) and highest in 2014 (3.16%; 95% CI: 2.10-4.22). Overall, the prevalence increased by 37% during the study period 2004 to 2014, but this difference was not statistically significant (OR 1.37; 95% CI: 0.77-2.45). The lifetime prevalence of subthreshold ADHD was considerably higher, with the lowest value in 2005 (9.23%; 95% CI 7.88-10.59) to 14.76 (95% CI: 12.72-16.79) in 2014, and increased significantly over time (p-value < .001).

[Insert Figure 1 about here]

Figure 2 shows the lifetime prevalence of diagnostic level (Figure 2A) and subthreshold (Figure 2B) ADHD during the study period separately for boys and girls (see Table S1 for exact numbers). The lifetime prevalence of both diagnostic level and of subthreshold ADHD

was consistently lower among girls compared to boys. Again, there was no statistically significant increase in diagnostic level ADHD over time in either boys or girls (p-values .229 and .865 respectively), whereas subthreshold ADHD increased significantly over time (p-value .017 for boys and .007 for girls).

[Insert Figure 2 about here]

There was also a significant increase in the mean ADHD scores among the study participants over time (Figure 3). The mean score on the total ADHD scale ranged from 1.79 (95% CI 1.69-1.88) in 2004 to 2.29 (95% CI 2.19-2.40) in 2014 (p-value < .001; β=0.05). A similar pattern was found when analyzing mean scores on the attention deficit/concentration and hyperactivity/impulsivity subscales (Table 2). These results were consistent across sex, although with boys constantly having higher scores than girls (Table S2, available online).

[Insert Figure 3 about here]

Repeating the analyses in a subsample of one randomly selected twin per pair resulted in similar estimates for diagnostic level ADHD as when the entire sample was analyzed, with no significant difference in the prevalence over time (p-value: 0.88), although with wider confidence intervals (Table S3, available online). Furthermore, there was no longer any significant difference in the prevalence of subthreshold ADHD over time (p-value: 0.403). There was a significant effect of year on mean ADHD scores (p-value: 0.0002), but it was no longer linear as the estimates seemed to fluctuate over time (Table S3).

Results from the sensitivity analysis of clinically diagnosed children in the National Patient Register showed that while there was a significant effect of baseline participation in CATSS (p-value .049), there was no significant interaction between year and participation in CATSS (p-value .365). This means that although participants differed significantly from non-participants with regard to receiving an ADHD diagnosis, this did not differ over time.

The lifetime prevalence of clinically diagnosed ADHD increased significantly over time (p-value < .001). The prevalence was 0.39 (95% CI 0.01-0.77) in 2004, and increased each year up until 2013 (prevalence: 2.28; 95% CI 1.52-3.04), to then level off slightly to 2.01 (95% CI 1.32-2.70) in 2014 (Table S4, available online). Overall, the lifetime prevalence of clinically diagnosed ADHD increased more than five-fold from 2004 to 2014 (OR 5.27, 95% CI 1.85-14.96).

DISCUSSION

The findings from this cross-sectional study suggest that the lifetime prevalence of ADHD-like traits at the extreme end of the distribution (corresponding to our category of ADHD diagnostic level) has been stable from 2004 to 2014 among nine year olds in Sweden. These results were consistent for boys and girls, with a consistently higher lifetime prevalence of ADHD in boys. This is in line with findings from the meta-analysis by Polanczyk et al. (2014) indicating that the prevalence of ADHD in non-referred samples was stable over a 30 year period. Similarly, a recent study of the prevalence of Autism Spectrum Disorders (ASD), based on the same data as the present study, has shown that the lifetime prevalence of the autism phenotype has been stable over time, contrary to previous reports of an increase in clinically diagnosed ASD (Lundstrom, Reichenberg, Anckarsater, Lichtenstein & Gillberg, 2015). Therefore, it seems unlikely that the increase found in studies based on clinical

diagnosis and/or treatment of ADHD would represent a true increase in the prevalence of the underlying ADHD phenotype. These findings rather suggest that the increase seen in clinical diagnosis and in prescription of ADHD medication might be caused by other factors, such as changes in diagnostic and treatment practices of ADHD, administrative changes in reporting diagnoses, greater awareness among physicians, parents and teachers, or better access to healthcare.

It is also possible that the increase previously seen in diagnosed ADHD might be caused by over-diagnosing, for instance due to changed administrative practices in schools where a diagnosis is now almost a prerequisite for financial support (Fernell, Landgren, Lindstrom, Johnson & Gillberg, 2013), and thus an incentive for school personnel to highlight referral as an option, or by neglect in ruling out other diagnoses, both psychiatric and somatic (such as metabolic imbalances or thyroid dysfunction). Furthermore, the impairment of symptoms is a prerequisite in the diagnostic criteria for ADHD, and a potential neglect to consider impairment would most likely result in considerably higher rates of ADHD.

It is possible that the increase found for subthreshold ADHD and mean scores might reflect an increase in the number of symptoms, where parents might rate their children to have more symptoms now compared with ten years ago. In general, knowledge about ADHD has increased during this time period, resulting in a larger familiarity and recognition of ADHD symptoms overall. It is important to note the rather small effect size – the mean scores increased with half a point on a scale ranging from 0 to 19, corresponding to an increase of half a symptom over a ten year study period. Many of the estimates also had overlapping confidence intervals. In addition, the total increase in the lifetime prevalence of diagnostic level ADHD during the entire study period (2004-2014) was minimal (1.37-fold increase),

compared with the more than five-fold increase seen in clinically diagnosed ADHD during the same time period. This can also be compared with previous studies on Swedish data, where the one-year prevalence increased more than four-fold from 2006 to 2011 (Giacobini et al., DOI: 10.1177/1087054714554617), the prevalence of clinically diagnosed ADHD among 10-year olds increased more than 7-fold from 1990 to 2007 (Atladottir et al., 2015), and the one-year prevalence of dispensed ADHD medication increased 2.28-fold from 2006 to 2009 (Zetterqvist et al., 2013). Therefore, it is unlikely that the small increase in the normal and sub-threshold variations of ADHD-like traits seen in this study explain the observed increase in clinically diagnosed ADHD.

The main strengths of this study include the large sample size, the relatively high response rate, the population-based sample, and the long study period. Furthermore, the instrument used to measure ADHD-like traits was based on DSM-IV criteria, has been stable over time, and has been shown to have good validity. There are some limitations that should be kept in mind when interpreting the results from this study. We were concerned that the decreasing participation rate in CATSS might have confounded our analyses as non-participants have been shown to have higher rates of ADHD (Anckarsäter et al., 2011), especially when taken together with the significant increase found regarding subthreshold ADHD and mean ADHD scores. However, findings from our sensitivity analysis, where we studied the potential effect of attrition on ADHD diagnosis, did not support this notion. The ADHD scale has been validated in several studies and consistently shown to have excellent specificity. The moderate sensitivity, however, might explain the relatively low rates of diagnostic level ADHD seen in this study. Another limitation of the moderate sensitivity is that we may have under-estimated changes over time; assuming that the statistically significant increase in ADHD symptoms generates an increase in the prevalence of ADHD cases that falls below our

strict criteria for ADHD. Furthermore, ADHD-traits were assess based on parental reports only, and did not take into account teacher reports, information about impairment or evaluate cross-context manifestations, although the measures were validated against clinical diagnoses where these aspects are taken into account. We did not take pharmacological treatment into account and there is a possibility that parents might have rated children undergoing medication as having fewer symptoms because of treatment, although few children were treated with ADHD medication (170 children had at least one filled prescription for ADHD medication during the year they turned nine) and questions were asked in a lifetime perspective. While these factors might explain the relatively low prevalence seen in this sample, they are unlikely to influence the pattern in prevalence over time. A further consideration regards the generalizability of results from a sample of twins to singletons. However, twins have been shown to be comparable to singletons with regard to traits of ADHD (Moilanen et al., 1999), supporting the generalizability of our results to singletons. If twins are more (or less) likely to be referred than singletons, and if this type of referral has changed over time, it might influence our results regarding clinically diagnosed ADHD. However, it seems unlikely that twins should require fewer ADHD-traits, than singletons, in order to be assigned a clinical diagnosis. Nevertheless, our study results need to be replicated in other settings using other study designs.

CONCLUSION

In this study, we found no evidence of an increase in the lifetime prevalence of ADHD-like traits at the extreme end of the distribution among nine-year olds during the period 2004-2014, while we cannot rule out a small increase in the normal and sub-threshold variations of ADHD-like traits. The increased rates of clinically diagnosed ADHD reported in previous studies might therefore be influenced by practical and political factors, such as changes in

diagnostic and treatment practices of ADHD, administrative changes in reporting diagnoses, greater awareness among physicians, parents and teachers, better access to healthcare, or current over-diagnosis of ADHD.

Key points

- Studies have reported increases in clinically diagnosed and treated ADHD, but it is unclear if this reflects an increase in the underlying ADHD phenotype.
- In this study of almost 20,000 nine-year old twins, the prevalence of diagnostic level ADHD did not differ significantly over time.
- Increased rates of clinically diagnosed ADHD cases in previous studies probably reflect changes in diagnostic and treatment practices of ADHD, administrative changes in reporting diagnoses, greater awareness of ADHD, better access to healthcare, or current over-diagnosis of ADHD, rather than an increase in the ADHD phenotype.

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REFERENCES

Anckarsäter, H., Lundström, S., Kollberg, L., Kerekes, N., Palm, C., Carlström, E., Långström, N., Magnusson, P. K., Halldner, L. & Bölte, S. (2011). The child and adolescent twin study in Sweden (CATSS). *Twin Research and Human Genetics,* 14**,** 495-508.

Atladottir, H. O., Gyllenberg, D., Langridge, A., Sandin, S., Hansen, S. N., Leonard, H., Gissler, M., Reichenberg, A., Schendel, D. E., Bourke, J., Hultman, C. M., Grice, D. E., Buxbaum, J. D. & Parner, E. T. (2015). The increasing prevalence of reported diagnoses of childhood psychiatric disorders: a descriptive multinational comparison. *European Child and Adolescent Psychiatry,* 24**,** 173-183.

Beau-Lejdstrom, R., Douglas, I., Evans, S. J. & Smeeth, L. (2016). Latest trends in ADHD drug prescribing patterns in children in the UK: prevalence, incidence and persistence. *BMJ Open,* 6**,** e010508.

Biederman, J. & Faraone, S. V. (2005). Attention-deficit hyperactivity disorder. *Lancet,* 366**,** 237-248.

Chien, I. C., Lin, C. H., Chou, Y. J. & Chou, P. (2012). Prevalence, incidence, and stimulant use of attention-deficit hyperactivity disorder in Taiwan, 1996-2005: a national population-based study. *Social Psychiatry and Psychiatric Epidemiology,* 47**,** 1885-1890.

Faraone, S. V., Sergeant, J., Gillberg, C. & Biederman, J. (2003). The worldwide prevalence of ADHD: is it an American condition. *World psychiatry,* 2**,** 104-113.

Fernell, E., Landgren, M., Lindstrom, K., Johnson, M. & Gillberg, C. (2013). Barn och unga med utvecklingsneurologiska problem: Stöd och insatser måste kunna ges även om inte alla diagnoskriterier är uppfyllda [Children and young people with neurodevelopmental problems: Support and efforts must be given even if not all diagnostic criteria are met]. *Lakartidningen*, 110**,** 1674.

Giacobini, M., Medin, E., Ahnemark, E., Russo, L. J. & Carlqvist, P. (DOI: 10.1177/1087054714554617). Prevalence, Patient Characteristics, and Pharmacological Treatment of Children, Adolescents, and Adults Diagnosed With ADHD in Sweden [published online ahead of print November 2014]. *J Atten Disord*.

Hansson, S. L., Svanstrom Rojvall, A., Rastam, M., Gillberg, C., Gillberg, C. & Anckarsater, H. (2005). Psychiatric telephone interview with parents for screening of childhood autism - tics, attention-deficit hyperactivity disorder and other comorbidities (A-TAC): preliminary reliability and validity. *British Journal of Psychiatry*, 187**,** 262-267.

Klein, R. G., Mannuzza, S., Olazagasti, M. A., Roizen, E., Hutchison, J. A., Lashua, E. C. & Castellanos, F. X. (2012). Clinical and functional outcome of childhood attention-deficit/hyperactivity disorder 33 years later. *Archives of General Psychiatry*, 69**,** 1295-1303.

Larson, T., Anckarsater, H., Gillberg, C., Stahlberg, O., Carlstrom, E., Kadesjo, B., Rastam, M., Lichtenstein, P. & Gillberg, C. (2010). The autism--tics, AD/HD and other comorbidities inventory (A-TAC): further validation of a telephone interview for epidemiological research. *BMC Psychiatry*, 10**,** 1.

Larson, T., Kerekes, N., Selinus, E. N., Lichtenstein, P., Gumpert, C. H., Anckarsater, H., Nilsson, T. & Lundstrom, S. (2014). Reliability of Autism-Tics, AD/HD, and other Comorbidities (A-TAC) inventory in a test-retest design. *Psychological Reports,* 114**,** 93-103.

Larson, T., Lundstrom, S., Nilsson, T., Selinus, E. N., Rastam, M., Lichtenstein, P., Gumpert, C. H., Anckarsater, H. & Kerekes, N. (2013). Predictive properties of the A-TAC inventory when screening for childhood-onset neurodevelopmental problems in a population-based sample. *BMC Psychiatry,* 13**,** 233.

Ludvigsson, J. F., Andersson, E., Ekbom, A., Feychting, M., Kim, J. L., Reuterwall, C., Heurgren, M. & Olausson, P. O. (2011). External review and validation of the Swedish national inpatient register. *BMC Public Health,* 11**,** 450.

Lundstrom, S., Reichenberg, A., Anckarsater, H., Lichtenstein, P. & Gillberg, C. (2015). Autism phenotype versus registered diagnosis in Swedish children: prevalence trends over 10 years in general population samples. *BMJ,* 350**,** h1961.

Moilanen, I., Linna, S.-L., Ebeling, H., Kumpulainen, K., Tamminen, T., Piha, J. & Almqvist, F. (1999). Are twins' behavioural/emotional problems different from singletons'? *European Child and Adolescent Psychiatry,* 8**,** S62-S67.

Polanczyk, G., de Lima, M. S., Horta, B. L., Biederman, J. & Rohde, L. A. (2007). The worldwide prevalence of ADHD: a systematic review and metaregression analysis. *The American journal of psychiatry,* 164**,** 942-948.

Polanczyk, G. V., Willcutt, E. G., Salum, G. A., Kieling, C. & Rohde, L. A. (2014). ADHD prevalence estimates across three decades: an updated systematic review and meta-regression analysis. *International Journal of Epidemiology,* 43**,** 434-442.

Renoux, C., Shin, J. Y., Dell'Aniello, S., Fergusson, E. & Suissa, S. (2016). Prescribing trends of attention-deficit hyperactivity disorder (ADHD) medications in UK primary care, 1995-2015. *British Journal of Clinical Pharmacology,* 82**,** 858-868.

Robison, L. M., Skaer, T. L., Sclar, D. A. & Galin, R. S. (2002). Is attention deficit hyperactivity disorder increasing among girls in the US? Trends in diagnosis and the prescribing of stimulants. *CNS Drugs,* 16**,** 129-137.

Safer, D. J. (DOI: 10.1177/1087054715586571). Is ADHD Really Increasing in Youth? [published online ahead of print June 2015]. *J Atten Disord*.

Sclar, D. A., Robison, L. M., Bowen, K. A., Schmidt, J. M., Castillo, L. V. & Oganov, A. M. (2012). Attention-deficit/hyperactivity disorder among children and adolescents in the United States: trend in diagnosis and use of pharmacotherapy by gender. *Clinical Pediatrics,* 51**,** 584-589.

Stefanski, L. A. & Boos, D. D. (2002). The calculus of M-estimation. *The American Statistician,* 56**,** 29-38.

Trip, A. M., Visser, S. T., Kalverdijk, L. J. & de Jong-van den Berg, L. T. (2009). Large increase of the use of psycho-stimulants among youth in the Netherlands between 1996 and 2006. *British Journal of Clinical Pharmacology,* 67**,** 466-468.

Visser, S. N., Danielson, M. L., Bitsko, R. H., Holbrook, J. R., Kogan, M. D., Ghandour, R. M., Perou, R. & Blumberg, S. J. (2014). Trends in the parent-report of health care provider-diagnosed and medicated attention-deficit/hyperactivity disorder: United States, 2003–2011. *Journal of the American Academy of Child and Adolescent Psychiatry,* 53**,** 34-46. e32.

Zetterqvist, J., Asherson, P., Halldner, L., Långström, N. & Larsson, H. (2013). Stimulant and non-stimulant attention deficit/hyperactivity disorder drug use: total population study of trends and discontinuation patterns 2006–2009. *Acta Psychiatrica Scandinavica,* 128**,** 70-77.

Zito, J. M., Safer, D. J., DosReis, S., Gardner, J. F., Magder, L., Soeken, K., Boles, M., Lynch, F. & Riddle, M. A. (2003). Psychotropic practice patterns for youth: a 10-year perspective. *Archives of Pediatrics and Adolescent Medicine,* 157**,** 17-25.

TABLES AND FIGURES

Table 1. Descriptive information about study participants.

	Birth year, categorized*					
	1995-1998 (n=6,876)		1999-2002 (n=7,628)		2003-2005 (n=4,767)	
Diagnostic level ADHD, n (%)	136	(2.0)	149	(2.0)	121	(2.5)
Subtreshold ADHD, n (%)	690	(10.0)	768	(10.1)	600	(12.6)
Sex						
Boys, n (%)	3521	(51.2)	3832	(50.2)	2406	(50.5)
Girls, n (%)	3355	(48.8)	3796	(49.8)	2361	(49.5)
Zygosity						
Monozygotic, n (%)	1871	(27.2)	1967	(25.8)	1362	(28.6)
Dizygotic, same sex, n (%)	2474	(36.0)	2672	(35.0)	1589	(33.3)
Dizygotic, opposite sex, n (%)	2387	(34.7)	2835	(37.2)	1661	(34.8)
Unknown, n (%)	144	(2.1)	154	(2.0)	155	(3.3)
Maternal age at child's birth						
25 years or younger, n (%)	874	(12.9)	708	(9.3)	385	(8.1)
26-30 years, n (%)	2440	(35.9)	2607	(34.2)	1462	(30.7)
31-35 years, n (%)	2494	(36.7)	2991	(39.2)	1836	(38.6)
36 years or older, n (%)	992	(14.6)	1317	(17.3)	1075	(22.6)
Mother's highest achieved education						
Primary and secondary education, n (%)	48	(5.3)	270	(3.7)	127	(2.8)
Upper secondary education, n (%)	341	(37.8)	2768	(37.9)	1362	(29.8)
Post-secondary education, n (%)	72	(8.0)	654	(8.9)	482	(10.6)
University education, n (%)	440	(48.8)	3621	(49.5)	2593	(56.8)
Father's highest achieved education						
Primary and secondary education, n (%)	70	(8.7)	495	(7.5)	242	(5.8)
Upper secondary education, n (%)	404	(50.2)	3231	(48.6)	1887	(45.1)
Post-secondary education, n (%)	36	(4.5)	412	(6.2)	369	(8.8)
University education, n (%)	294	(36.6)	2504	(37.7)	1690	(40.4)
Mother's country of birth						
Sweden, n (%)	6155	(89.8)	6889	(90.5)	4236	(89.0)
Other country, n (%)	699	(10.2)	720	(9.5)	524	(11.0)
Father's country of birth						
Sweden, n (%)	6077	(88.7)	6783	(89.3)	4224	(88.7)
Other country, n (%)	773	(11.3)	812	(10.7)	536	(11.3)

Note: ADHD = attention deficit hyperactivity disorder

* Data was collected on a yearly bases, but collapsed into categories for this table

Table 2. Lifetime prevalence of ADHD, subthreshold ADHD, clinically diagnosed ADHD, and mean ADHD scores among nine-year olds in Sweden 2004-2014.

	Prevalence (95% CI)		Mean scores (95% CI)		
Year	Diagnostic level ADHD	Subthreshold ADHD	ADHD	Attention deficit/ concentration	Hyperactivity/ impulsivity
2004	2.32 (1.27-3.37)	10.83 (8.83-12.84)	1.79 (1.69-1.88)	0.89 (0.84-0.94)	0.90 (0.84-0.95)
2005	1.60 (0.98-2.22)	9.23 (7.88-10.59)	1.84 (1.76-1.92)	0.92 (0.88-0.97)	0.92 (0.87-0.96)
2006	2.00 (1.36-2.65)	9.62 (8.21-11.03)	1.89 (1.82-1.96)	0.95 (0.91-0.99)	0.94 (0.90-0.98)
2007	2.16 (1.42-2.89)	10.88 (9.34-12.43)	1.94 (1.88-2.00)	0.98 (0.95-1.01)	0.96 (0.93-0.99)
2008	2.16 (1.50-2.82)	10.74 (9.22-12.25)	1.99 (1.94-2.04)	1.01 (0.98-1.04)	0.98 (0.95-1.01)
2009	1.42 (0.82-2.01)	9.37 (7.92-10.83)	2.04 (1.99-2.09)	1.04 (1.01-1.07)	1.00 (0.97-1.03)
2010	1.82 (1.15-2.48)	9.45 (8.00-10.90)	2.09 (2.04-2.15)	1.07 (1.04-1.10)	1.02 (0.99-1.05)
2011	2.39 (1.65-3.12)	10.64 (9.12-12.15)	2.14 (2.08-2.20)	1.10 (1.07-1.14)	1.04 (1.01-1.08)
2012	2.28 (1.57-2.99)	10.93 (9.42-12.45)	2.19 (2.12-2.27)	1.13 (1.09-1.17)	1.06 (1.02-1.10)
2013	2.31 (1.52-3.10)	12.81 (10.91-14.71)	2.24 (2.15-2.33)	1.16(1.11-1.21)	1.09 (1.04-1.13)
2014	3.16 (2.10-4.22)	14.76 (12.72-16.79)	2.29 (2.19-2.40)	1.19 (1.13-1.25)	1.11 (1.05-1.16)

Note: ADHD = attention deficit hyperactivity disorder; CI = Confidence Interval

Figure 1. Lifetime prevalence of diagnostic level and subthreshold ADHD among nine-year olds in Sweden 2004-2014.

Note: ADHD = attention deficit hyperactivity disorder

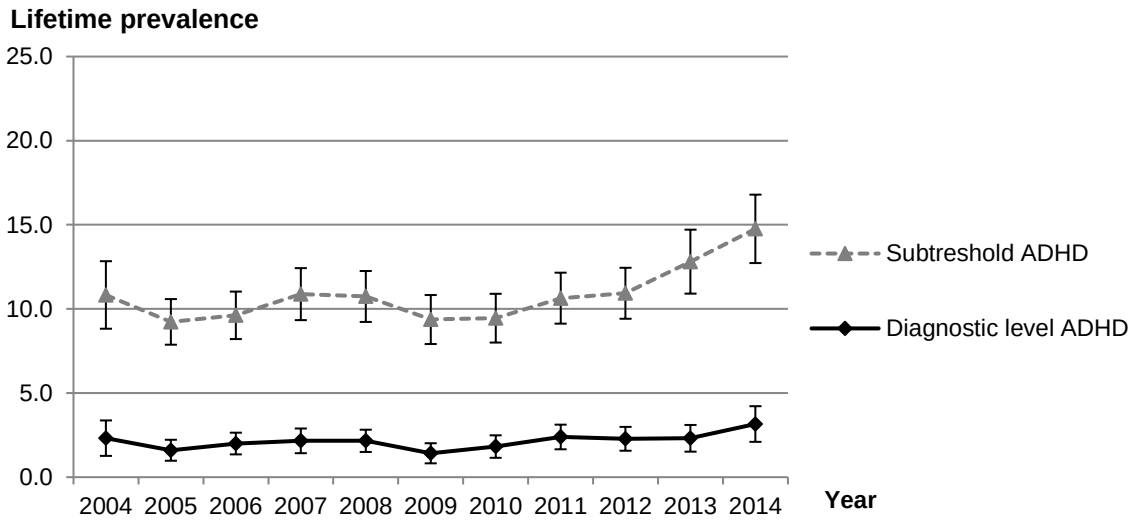


Figure 2. Lifetime prevalence of (A*)* diagnostic level and (B) subthreshold ADHD among nine-year olds in Sweden 2004-2014, shown separately for boys and girls.

Note: ADHD = attention deficit hyperactivity disorder

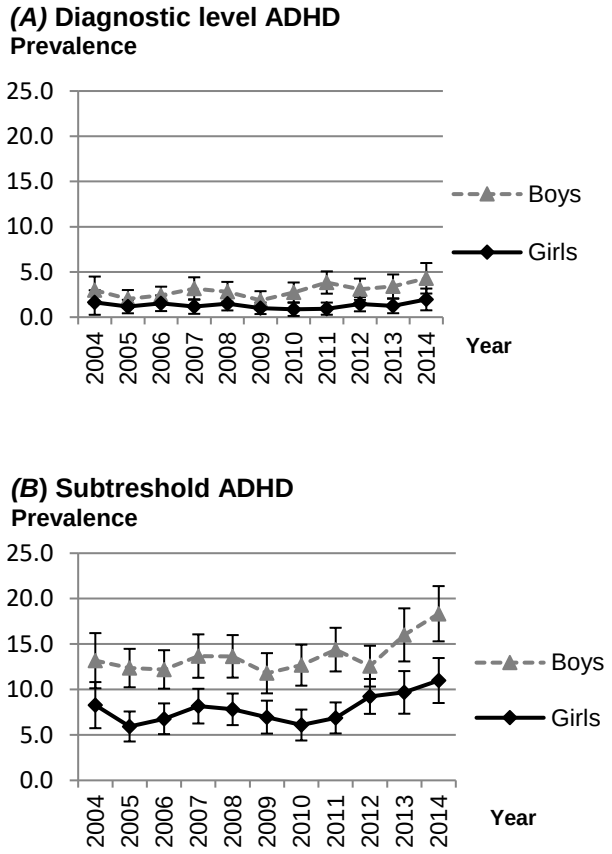
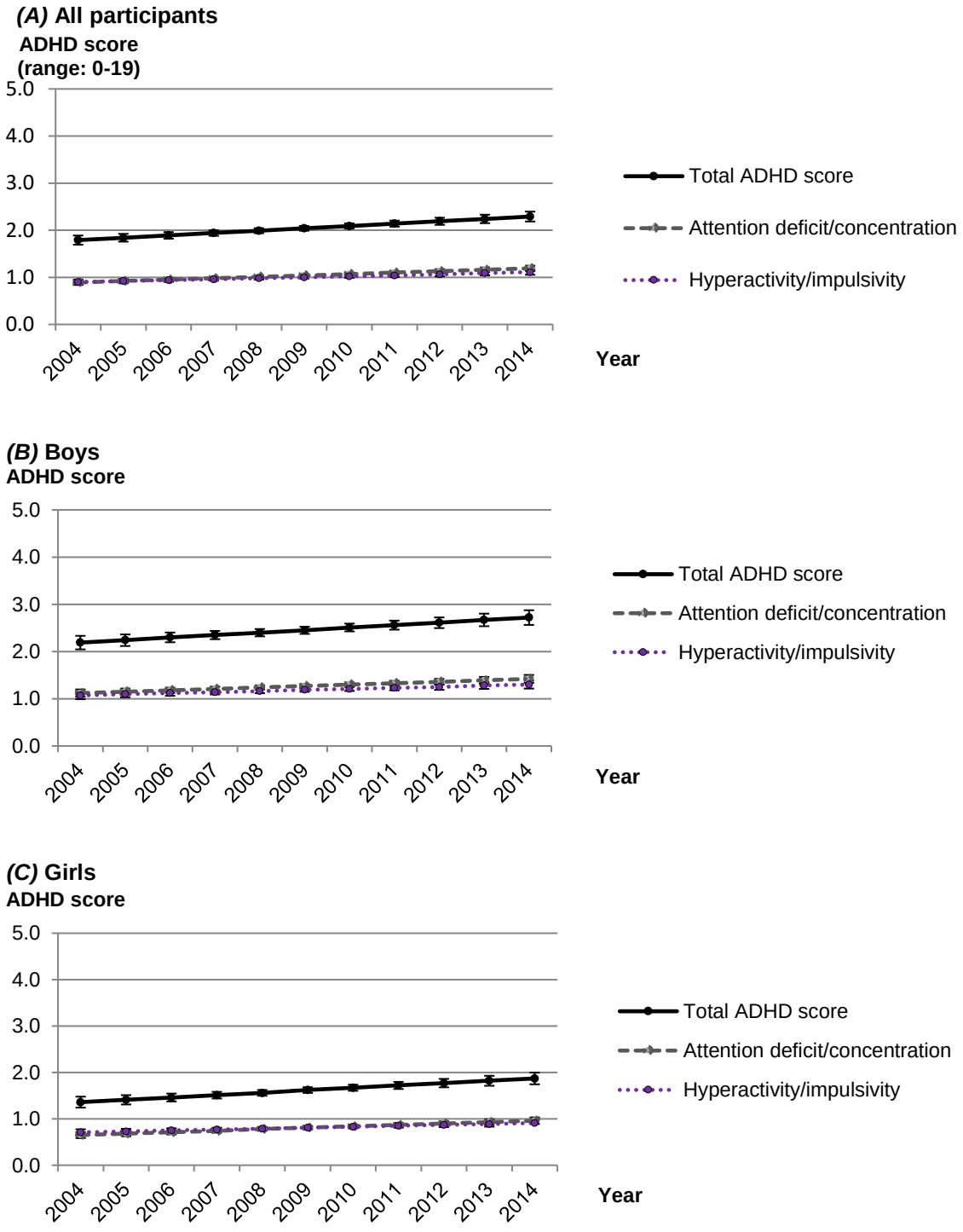


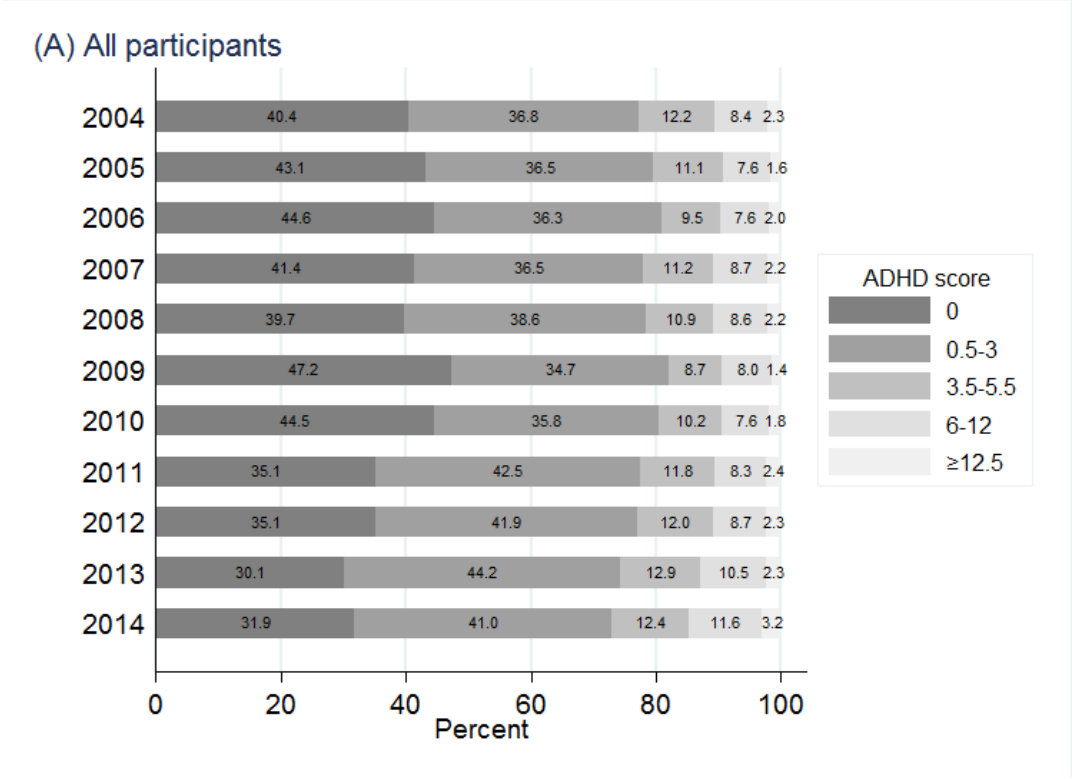
Figure 3. Mean ADHD score among nine-year olds in Sweden 2004-2014. Total ADHD score as well as divided by subtype (attention deficit/concentration and hyperactivity/impulsivity), shown for (A) all participants as well as separately for (B) boys and (C) girls.

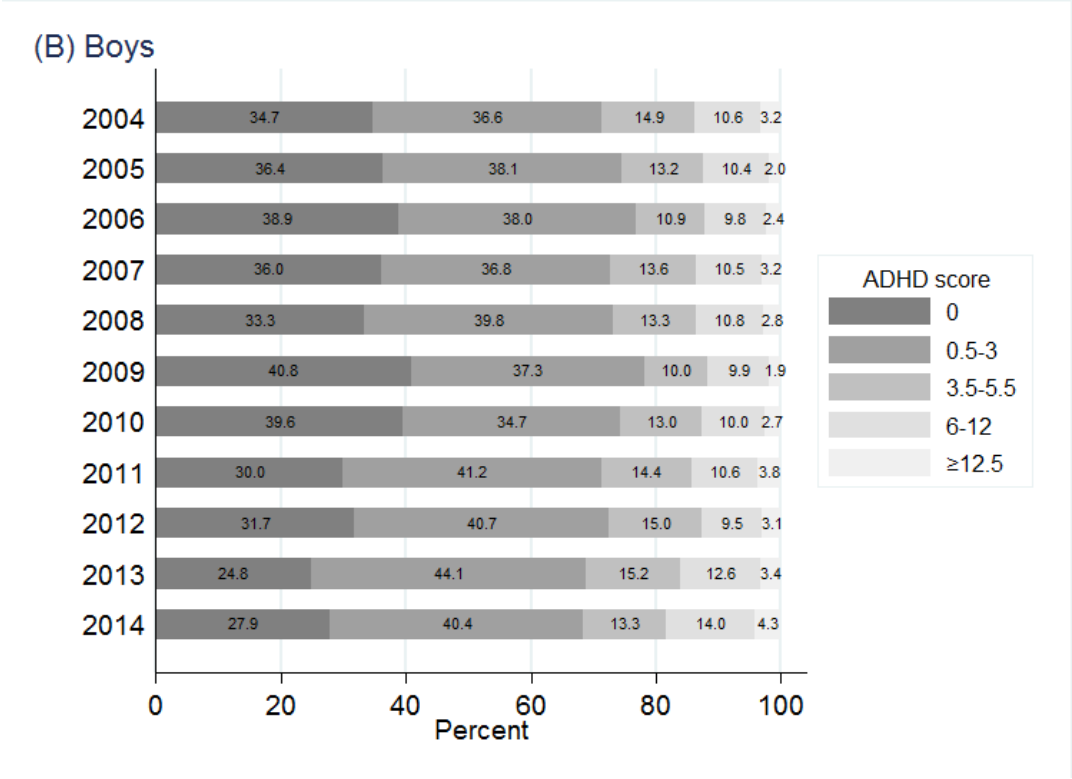
Note: ADHD = attention deficit hyperactivity disorder

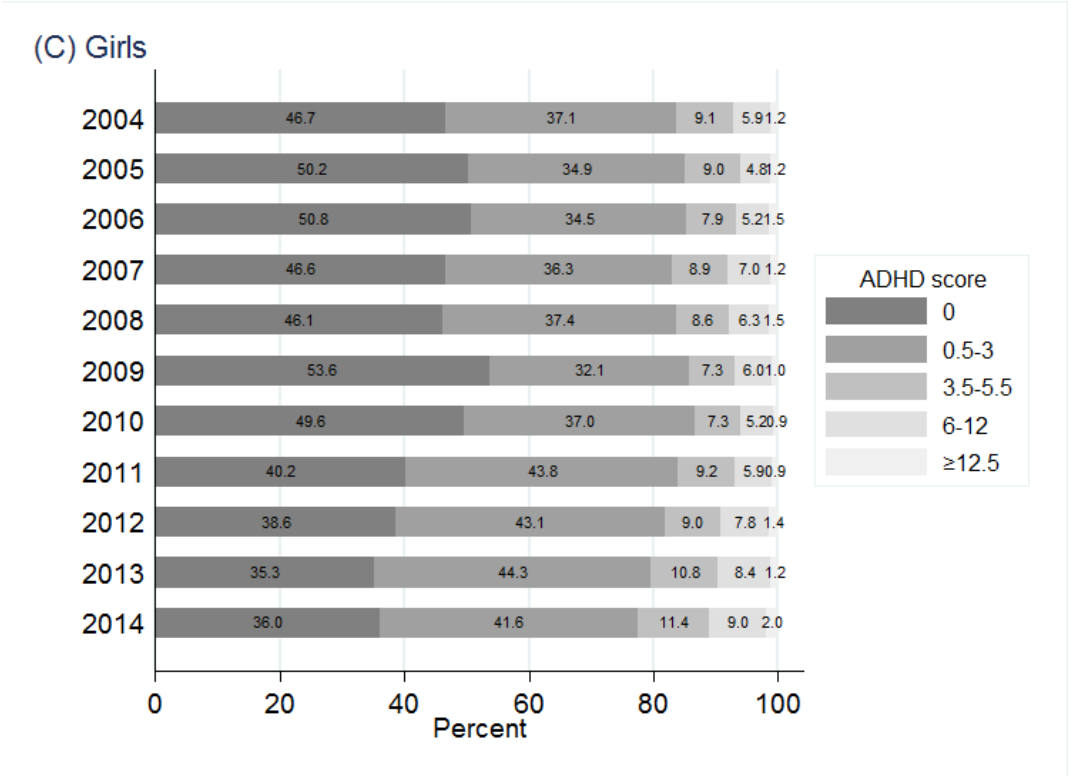


SUPPLEMENTARY MATERIAL

Supplementary Figure 1. Distribution of ADHD scores among participants across the study period 2004-2014, shown for (A) all participants, and separately for (B) boys and (C) girls.






(C) Girls
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
46.7 37.1 9.1 5.9 1.2
50.2 34.9 9.0 4.8 1.2
50.8 34.5 7.9 5.2 1.5
46.6 36.3 8.9 7.0 1.2
46.1 37.4 8.6 6.3 1.5
53.6 32.1 7.3 6.0 1.0
49.6 37.0 7.3 5.2 0.9
40.2 43.8 9.2 5.9 0.9
38.6 43.1 9.0 7.8 1.4
35.3 44.3 10.8 8.4 1.2
36.0 41.6 11.4 9.0 2.0
0
20
40
60
80
100
Percent
ADHD score
0
0.5-3
3.5-5.5
6-12
≥12.5

Supplementary Table 1. Lifetime prevalence of diagnostic level and subthreshold ADHD among nine-year olds in Sweden 2004-2014, shown separately for boys and girls

		Diagnostic level ADHD (95% CI)		**Subthreshold ADHD (95% CI)**	
Year	No of participants	Boys	Girls	Boys	Girls
2004	1,034	2.97 (1.45-4.49)	1.62 (0.26-2.97)	13.17 (10.14-16.21)	8.28 (5.75-10.82)
2005	1,939	2.01 (1.02-3.00)	1.17 (0.42-1.91)	12.36 (10.25-14.48)	5.93 (4.28-7.58)
2006	2,047	2.42 (1.47-3.37)	1.54 (0.67-2.41)	12.21 (10.09-14.33)	6.78 (5.08-8.47)
2007	1,856	3.17 (1.93-4.41)	1.17 (0.37-1.97)	13.68 (11.29-16.07)	8.17 (6.27-10.08)
2008	1,993	2.81 (1.72-3.90)	1.50 (0.75-2.26)	13.65 (11.31-16.00)	7.82 (6.09-9.56)
2009	1,835	1.86 (0.84-2.87)	0.98 (0.34-1.61)	11.79 (9.58-14.00)	6.96 (5.15-8.78)
2010	1,873	2.73 (1.62-3.83)	0.87 (0.14-1.60)	12.68 (10.43-14.94)	6.09 (4.39-7.80)
2011	1,927	3.83 (2.60-5.06)	0.94 (0.26-1.61)	14.39 (11.99-16.76)	6.87 (5.16-8.58)
2012	1,976	3.09 (1.92-4.27)	1.44 (0.64-2.23)	12.57 (10.33-14.82)	9.24 (7.32-11.16)
2013	1,429	3.40 (2.08-4.72)	1.24 (0.44-2.05)	16.01 (13.08-18.93)	9.68 (7.34-12.03)
2014	1,362	4.30 (2.61-5.98)	1.96 (0.75-3.16)	18.34 (15.30-21.38)	10.99 (8.52-13.47)

Note: ADHD = attention deficit hyperactivity disorder; CI = Confidence Interval

Supplementary Table 2. Mean ADHD score among nine-year olds in Sweden 2004-2014. Total score as well as divided by subtype (attention deficit/concentration and hyperactivity/impulsivity), shown separately for boys and girls

	Mean scores (95% CI)											
	ADHD				Attention deficit/concentration				Hyperactivity/impulsivity			
Year	Boys		Girls		Boys		Girls		Boys		Girls	
2004	2.19	(2.05-2.33)	1.36	(1.24-1.48)	1.12	(1.04-1.20)	0.65	(0.59-0.72)	1.07	(0.99-1.15)	0.71	(0.65-0.77)
2005	2.24	(2.12-2.37)	1.41	(1.31-1.51)	1.15	(1.08-1.22)	0.68	(0.63-0.74)	1.10	(1.03-1.16)	0.73	(0.68-0.78)
2006	2.30	(2.19-2.40)	1.46	(1.38-1.55)	1.18	(1.12-1.24)	0.71	(0.67-0.76)	1.12	(1.06-1.17)	0.75	(0.70-0.80)
2007	2.35	(2.26-2.44)	1.51	(1.44-1.59)	1.21	(1.16-1.26)	0.74	(0.71-0.78)	1.14	(1.09-1.19)	0.77	(0.73-0.81)
2008	2.40	(2.32-2.48)	1.56	(1.50-1.63)	1.24	(1.20-1.28)	0.78	(0.74-0.81)	1.16	(1.12-1.21)	0.79	(0.76-0.83)
2009	2.45	(2.38-2.53)	1.62	(1.55-1.68)	1.27	(1.23-1.31)	0.81	(0.77-0.84)	1.19	(1.14-1.23)	0.81	(0.78-0.84)
2010	2.51	(2.42-2.59)	1.67	(1.60-1.73)	1.30	(1.26-1.35)	0.84	(0.80-0.87)	1.21	(1.16-1.25)	0.83	(0.80-0.87)
2011	2.56	(2.46-2.65)	1.72	(1.64-1.79)	1.33	(1.28-1.38)	0.87	(0.82-0.91)	1.23	(1.18-1.28)	0.85	(0.81-0.89)
2012	2.61	(2.50-2.73)	1.77	(1.68-1.86)	1.36	(1.30-1.42)	0.90	(0.85-0.95)	1.25	(1.19-1.31)	0.87	(0.82-0.92)
2013	2.67	(2.53-2.80)	1.82	(1.71-1.92)	1.39	(1.32-1.47)	0.93	(0.87-0.99)	1.28	(1.20-1.35)	0.89	(0.83-0.95)
2014	2.72	(2.56-2.87)	1.87	(1.74-1.99)	1.42	(1.34-1.51)	0.96	(0.89-1.03)	1.30	(1.21-1.38)	0.91	(0.84-0.98)

Note: ADHD = attention deficit hyperactivity disorder; CI = Confidence Interval

Supplementary Table 3. Lifetime prevalence of diagnostic level and subthreshold ADHD, and mean ADHD score, among nine-year olds in Sweden 2004-2014. Results based on one randomly selected twin per pair.

	Diagnostic level ADHD		Subthreshold ADHD		ADHD score	
Year	Prevalence	(95% CI)	Prevalence	(95% CI)	Mean	(95% CI)
2004	2.68	(1.30-4.07)	11.30	(8.59-14.02)	2.24	(1.98-2.50)
2005	1.75	(0.92-2.57)	9.55	(7.70-11.39)	1.87	(1.68-2.07)
2006	1.66	(0.88-2.44)	10.05	(8.21-11.89)	1.84	(1.65-2.03)
2007	1.93	(1.05-2.82)	12.14	(10.04-14.24)	2.07	(1.87-2.26)
2008	2.10	(1.21-2.99)	10.79	(8.87-12.71)	2.06	(1.87-2.25)
2009	1.41	(0.65-2.17)	8.45	(6.66-10.25)	1.66	(1.47-1.86)
2010	2.02	(1.12-2.92)	10.21	(8.28-12.15)	1.92	(1.72-2.11)
2011	2.28	(1.34-3.21)	10.75	(8.80-12.71)	2.14	(1.94-2.33)
2012	1.92	(1.06-2.77)	11.40	(9.42-13.38)	2.12	(1.93-2.31)
2013	2.37	(1.26-3.48)	11.58	(9.23-13.92)	2.30	(2.07-2.52)
2014	2.35	(1.21-3.48)	11.29	(8.92-13.67)	2.24	(2.01-2.47)

Note: ADHD = attention deficit hyperactivity disorder; CI = Confidence Interval

Supplementary Table 4. Lifetime prevalence of clinically diagnosed ADHD among nine-year old twins participating in the Child and Adolescent Twin Study in Sweden 2004-2014

	Clinically diagnosed ADHD		
Year	No of diagnosed children	Prevalence	(95% CI)
2004	4	0.39	(0.01-0.77)
2005	13	0.69	(0.31-1.06)
2006	19	0.98	(0.54-1.42)
2007	14	0.79	(0.38-1.21)
2008	19	1.00	(0.55-1.45)
2009	21	1.19	(0.68-1.69)
2010	31	1.75	(1.14-2.36)
2011	35	1.82	(1.22-2.42)
2012	39	1.97	(1.36-2.59)
2013	34	2.28	(1.52-3.04)

Note: ADHD = attention deficit hyperactivity disorder; CI = Confidence Interval